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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,366	01/18/2002	C. Alexander Kamb	VEN-9 CIP CON	4183

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BINGHAM MCCUTCHEN
THREE EMBARCADERO CENTER
SUITE 1800
SAN FRANCISCO, CA 94111

EXAMINER

FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 05/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/053,366

Applicant(s)

KAMB, C. ALEXANDER

Examiner

Jeffrey Fredman

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-31 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other: ____.

DETAILED ACTION

Priority

1. Applicant's claim for domestic priority under 35 U.S.C. 120 is acknowledged. However, the application upon which the continuation in part priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-31 of this application.

Specifically, as noted in the prosecution of parent application 08/764,191

"Claims 65 and its dependent claims are drawn to a method where a nucleic acid sample is propagated through a cell and then compared for changes to the starting material. A description of this invention was not found in the specification, and particularly was not found in the cited locations of pages 38-42 and original claims 21 and 22. Original claims 21 and 22 clearly are drawn to the embodiment where the nucleic acids are propagated through two different cells and the resultant products compared. These claims include no discussion of a comparison with the starting material. Also, page 38-42 of the specification entirely focus upon comparison of nucleic acids propagated through two different cell lines. As example 16 also demonstrates, on pages 57-59, the specification solely contemplates comparison of two different cell lines and not a comparison of the resultant product to the starting material. (In final rejection)".

Therefore, the current claims do not receive priority to the parent application as the parent application lacks descriptive support for these claims.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Pestov et al (Proc. Natl. Acad. Sci. (1994) 91:12549-12553).

Pestov teaches a method of identifying cDNA agents which kill or arrest growth in a cell (abstract) comprising: a) introducing an initial cDNA genetic library of putative negative selection agents into a cell population (page 12550, column 1), b) propagating the cell population some members of which cell population have a phenotype that is altered by the library agents (page 12550, column 1 and page 12551, figure 3), c) re-isolating the library components from the propagated cell population (page 12550, column 1), repeating steps a)-c) multiple times (page 12550, column 2), and d) subjecting the initial and re-isolated components to a quantitative comparison of the relative amounts of at least one specific library component (page 12551, figure 3).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pestov in view of Schena et al (Science (1995) 270:467-470).

Pestov teaches a method of identifying cDNA agents which kill or arrest growth in a cell (abstract) comprising: a) introducing an initial cDNA genetic library of putative negative selection agents into a cell population (page 12550, column 1), b) propagating the cell population so some members of which have a phenotype that is altered by the library agents (page 12550, column 1 and page 12551, figure 3), c) re-isolating the library components from the propagated cell population (page 12550, column 1), repeating steps a)-c) multiple times (page 12550, column 2), and d) subjecting the initial and re-isolated components to a quantitative comparison of the relative amounts of at least one specific library component (page 12551, figure 3).

Pestov does not teach the use of capture probes of 10-100 nucleotides for comparison of the two components.

Schena teaches a method for comparing relative amounts of nucleic acids in two samples comprising the steps: a) generating a pool of first wildtype fluorescein (FITC) labeled samples and second HAT4 lissamine labeled samples (page 468, column 3, paragraph 2), b) contacting the two pools with a plurality of solid supports with attached nucleic acids under conditions of hybridization (page 468, column 3, paragraph 2 and page 467, column 3), c) sorting the solid supports according to the relative amounts of first and second label (page 468, figure 1), d) determining the identity of nucleic acid molecules having the relative amount of first and second label (page 468, column 3, paragraph 2 and figures 1 and 2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the comparison method of Pestov with the use of arrays as taught by Schena since Schena notes "A high-capacity system was

developed to monitor the expression of many genes in parallel. Microarrays prepared by high-speed robotic printing of complementary DNAs on glass were used for quantitative expression measurements of the corresponding genes. Because of the small format and high density of the arrays, hybridization volumes of 2 microliters could be used that enabled detection of rare transcripts in probe mixtures derived from 2 micrograms of total cellular messenger RNA. (Abstract)." An ordinary practitioner would have been motivated to compare the different libraries of Pestov using the method of Schena in order to be able to detect rare transcripts, in a quantitative manner with a high capacity system.

6. Claims 1-14 and 21-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pestov in view of Schena et al (Science (1995) 270:467-470) and further in view of Brenner (U.S. Patent 5,604,097) and further in view of Brenner et al (Proc. Natl. Acad. Sci. (1992) 89:5381-5383).

Pestov in view of Schena teach the limitations of claims 1-8 as discussed above. Pestov in view of Schena do not teach the use of tags.

Brenner (U.S. Patent 5,604,097) teaches methods of using sequence identifier tags composed of 3-mer to 6-mer motifs in combination (columns 7 and 8) which may be attached to beads or other solid supports (column 12, line 40 to column 14, line 5). Brenner (U.S. Patent 5,604,097) further teaches sorting the polynucleotides in nucleic acid analytical methods such as RNA and DNA sequences and mRNA fingerprinting (abstract) as well as teaching lengths from 12 to 60 nucleotides (column 9, lines 14-21).

Brenner et al (Proc. Natl. Acad. Sci.) teaches that the size of the combinatorial library may be extended, if necessary (page 5382, column 2, paragraph 2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the comparison method of Pestov in view of Schena with the tags of Brenner (U.S. Patent 5,604,097) and Brenner et al (Proc. Natl. Acad. Sci.) since Brenner (U.S. Patent 5,604,097) states "The invention is particularly useful in labeling and sorting polynucleotides for parallel operations such as sequencing, fingerprinting or other types of analysis (column 6, lines 26-29)". The ordinary practitioner would have been motivated to use longer units in tandem configuration since Brenner (Proc. Natl. Acad. Sci.) states "The complexity of the combinatorial library is d^n . Libraries with a smaller degree, say $d=3$, should be coded by sextuplets, which, in the simplest case could be a repeated triplet (this size is chosen because any combination of triplets still obeys the commaless condition). In the same way, the size of the alphabet can be extended by using combinations of triplets to code for chemical units (page 5382, column 2, paragraph 2)". This explicit teaching motivates the use, at a minimum, of 9-mer units since 9-mers would retain the commaless conditions (as would 12-mers and so on). An ordinary practitioner would be further motivated to use longer sequences in complex mixtures since it is well known in the art that a longer, perfectly matching nucleic acid sequence hybridizes more efficiently and with greater specificity than a shorter perfectly matching nucleic acid sequence.

7. Claims 1-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pestov in view of Schena et al (Science (1995) 270:467-470) and further in view of Brenner (U.S. Patent 5,604,097) and further in view of Brenner et al (Proc. Natl. Acad. Sci. (1992) 89:5381-5383) and further in view of Kamb et al (U.S. Patent 5,955,275).

Pestov in view of Schena and further in view of Brenner (U.S. Patent 5,604,097) and further in view of Brenner (Proc. Natl. Acad. Sci.) teach the limitations of claims 1-14, 21-31 as discussed above. Pestov in view of Schena and further in view of Brenner (U.S. Patent 5,604,097) and further in view of Brenner (Proc. Natl. Acad. Sci.) do not teach the use of multiple mixed cell types or multiple lead compounds or the use of a flow sorter.

Kamb et al teaches the use of multiple cell types which may be the same or different (claims 21-28) as well as multiple types of lead compounds (column 17, subheading "Small Molecule Displacement Screen based on Perturbagen-Target Interactions") and the use of a flow sorter (example 3).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the comparison method of Pestov in view of Schena and further in view of Brenner (U.S. Patent 5,604,097) and further in view of Brenner (Proc. Natl. Acad. Sci.) with the perturbagen method of Kamb since Kamb states " The method should be simple, rapid, and permit identification of components of genetic pathways that regulate traits of interest. It should circumvent many of the obstacles that have interfered with genetic analysis in certain cells and organisms. It should not require an understanding of the detailed basis of a particular phenotype, or the mechanisms that underlie specific cellular behaviors. The method should be generally applicable to a great variety of cells, including cells cultured from somatic tissues of multicellular organisms, and it should sidestep certain disadvantages of somatic cell genetics, including the diploid character of most cells, the difficulty of isolating mutant genes once mutations have been induced, and the heterogeneity of


many cell populations. (Column 2, lines 54 To 67)." An ordinary practitioner would have been motivated to combine these methods for the benefits expressly indicated of improved simplicity and speed combined with the applicability to a wide variety of cells.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Jeffrey Fredman
Primary Examiner
Art Unit 1634

May 1, 2003